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Comparison of Sublingual, Vaginal and Oral Misoprostol in Cervical Ripening Prior to 1st Trimester Surgical Abortion a Prospective Study

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Abstract

Aim: *Comparison of sublingual, vaginal and oral misoprostol as a cervical ripening agent 4 hours prior to surgical abortion*

Objective: *To compare effectiveness and tolerability of misoprostol as cervical ripening agent in 1st trimester surgical abortion through different routes.*

Materials And Methods: *Hospital based prospective randomized study in which 144 women were divided into 3 groups sublingual, vaginal and oral group and single dose 400µg misoprostol was administered 4 hours prior to evacuation. Efficacy was assessed on the basis of dilation achieved and duration of procedure, the tolerability was evaluated based on the side effects.*

Results: *Cervical dilatation achieved in sublingual group was better than the other routes and had statistical significance. Duration of procedure was also lesser in sublingual group compared to oral and vaginal group. Side effects were seen in all groups, but vomiting being more common in oral group, nausea and uterine cramps more common in vaginal group and loose motion was seen only in sublingual group.*

Conclusion; *Administration of misoprostol by sublingual route is better than the oral and vaginal routes for cervical ripening.*

***Key words**: cervical ripening, misoprostol, dilation, side effects, first trimester abortion*

INTRODUCTION

Pregnancy is an important milestone of every woman's life. It is her right to decide how many children she wants to have. To help her in this regard, many contraceptive methods are available. However, when these methods fail, she will face an unintended pregnancy where she needs medical termination of pregnancy.

MTP was legalized in 1971. Most commonly used method is suction evacuation or dilatation and curettage of products of conception following mechanical dilatation of cervix. But mechanical dilatation has its own complications like uterine perforation, cervical laceration and cervical incompetence.[1, 2] Therefore, there aroused a need for a cervical priming agent to reduce these

complications.

In the treatment of abortion prostaglandins brought a revolution.[76] Among them prostaglandin E1 (misoprostol) became popular because of, easy availability stability at the room temperature, availability in different forms, easy administration, cost effectiveness, less cervical injuries and minimal intraoperative blood loss [4-6]

Many studies were carried out in different parts of the world to compare the effectiveness of misoprostol as cervical priming agent by different routes before 1st trimester surgical abortion.[77-81] However, in India studies are very few.[82]

The purpose of the current study is to compare the effectiveness and tolerability of misoprostol as a cervical priming agent given by different routes like sublingual, vaginal and oral prior to 1st trimester surgical abortion.

AIMS AND OBJECTIVES

Aim

Comparison of sublingual, oral and vaginal misoprostol 400 microgram as a cervical priming agent 4 hours prior to a surgical abortion.

Objective

To compare the efficacy and tolerability of tablet misoprostol 400 µg as a cervical ripening agent given 4 hours prior to a surgical abortion by one of the following routes:

i. sub lingual
ii. oral
iii. vaginal

MATERIALS AND METHODS

Materials

1) Study population: Patients with a history of amenorrhea who give consent for surgical abortion up to a period of gestation of 12 weeks will be enrolled and given tablet misoprostol 400 µg 4 hours prior to the surgical abortion by one of the following routes:
   i. sub lingual
   ii. oral
   iii. vaginal
2) Study design: Prospective randomized non blinded study.
3) Study place: Government Lady Goschen Hospital, Mangalore.
4) Sample size: $n=\frac{2(Z_\alpha + Z_\beta)^2 \times \sigma^2}{\Delta^2}$

   Z_α = 1.96 at 95% confidence level

   Z_β = 1.00 at 85% power

   Study size comes to be 144 (48 cases in each group).
5) Period of study: One and a half years (January 15 ,2014 to September 15, 2015).
6) Inclusion criteria:
   1) Pregnancy < 12 weeks period of gestation
   2) Patients willing to give informed consent
   3) Patients with os closed on examination
7) Exclusion criteria:
   1) Patients with complaints of vaginal bleeding
   2) History of allergy to prostaglandins
   3) Serum hemoglobin (Hb) < 9 g/dL
   4) History of any heart disease

Method

1. Informed consent was taken from all patients
2. Period of gestation was calculated from the last menstrual period (LMP).
3. A detailed history was taken and an examination including a per speculum and a per vaginal examination was done.
4. An ultrasonography (obstetrics USG) examination was done.
5. Vitals had been recorded before the procedure.
6. Routine investigations will include:
   i. Hb estimation
   ii. Blood grouping with Rh typing
   iii. Urine routine examination
   iv. HIV and HBsAg
7. After randomization by envelope method, 400 µg of tablet misoprostol will be given

either sublingually, orally or vaginally prior to the surgical abortion.

- Statistical analysis: Study results analyzed using SPSS version 17.0 by:
- Chi –square test
- ANOVA

The difference would be considered significant if 'p' value < 0.05.

Outcome measures

1. Efficacy:
   i. Dilatation of cervix achieved: Measured by passing Hegar's dilator in the descending order of size starting with Hegar's dilator number 12. The size of the largest Hegar's dilator that passed through the cervical os easily without resistance was considered as baseline dilatation.
   ii. Duration of the procedure:
   iii. From the time of introducing the dilator till the time of taking out of curette.
2. Tolerability:
   i. Uterine cramps
   ii. Loose motions
   iii. Nausea
   iv. Vomiting

RESULTS

EPIDEMILOGICAL AND OBSTETRIC PROFILE OF PATIENTS

	SUBLINGUAL	ORAL	VAGINAL	RESULT
AGE(YRS)	25.38+3.96	25.97+4.29	25.55+3.61	0.752NS
PARITY	2.4+ 0	2.4+ 0	2.4+ 0	NS
PERIOD OF GESTATION	7.65+ 1.87	7.58 + 2.05	8.27 + 1.92	0.165NS

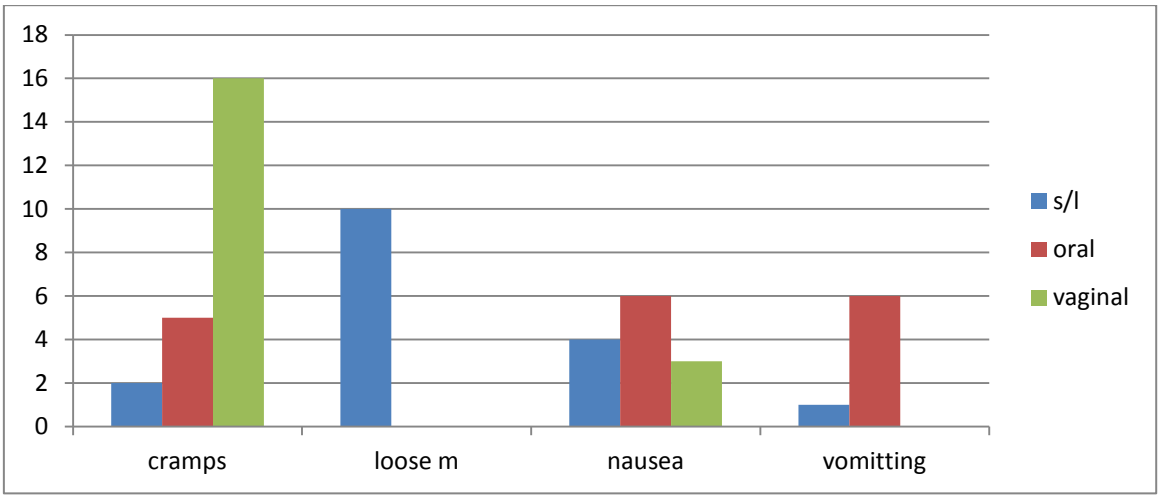
The values are expressed in mean

COMPARISON OF DIFFERENT PARAMETERS IN PATIENTS ADMINISTERED 400 MICROO GRAM OF MISOPROSTOL BY DIFFERENT ROUTES

	SUBLINGUAL	ORAL	VAGINAL	
CERVICAL DILATION(MM)	3.15	2.92	2.44	SIG
DURATION(MINUTES)	10.33	11.38	11.68	SIG
ABDOMINAL CRAMPS	4.2	10.4	33.3	SIG
LOOSE MOTIONS	20.8	0	0	SIG
NAUSEA	8.3	12.5	6.3	NS
VOMITING	2.1	12.5	O	SIG

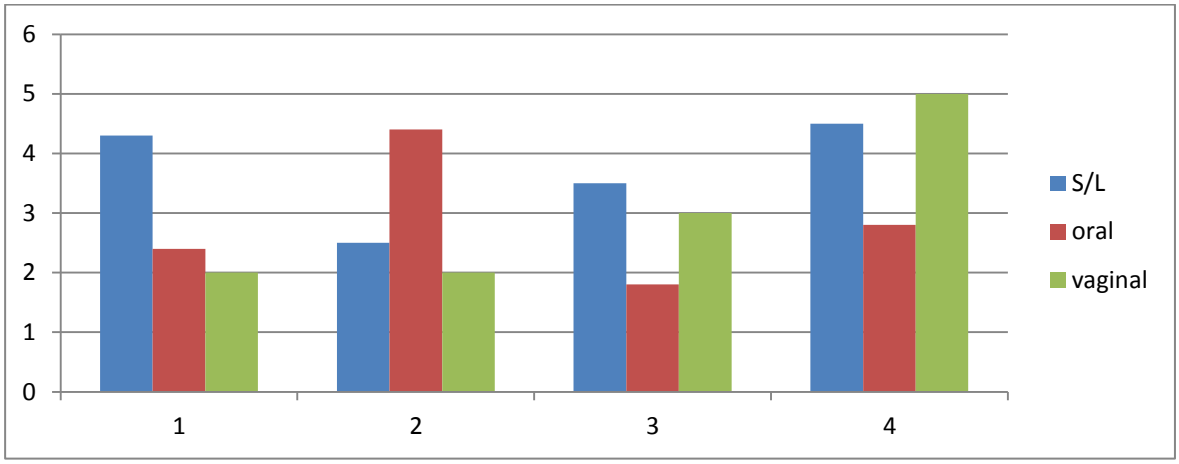
In case of abdominal cramps, loose motion and vomiting $p<0.05$, cervical dilation $P=0.0001$ Sig, duration $P=0.045$ Sig

GRAPHICAL REPRESENTATION OF DISTRIBUTION OF PATIENTS ACCORDING TO SIDE EFFECTS



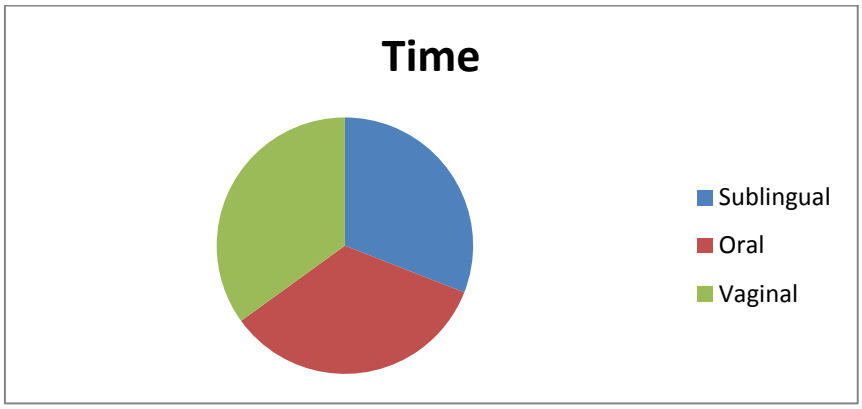
In sublingual group loose motion seen in 10(20.8%) patients followed by nausea in 4(8.3%) patients. In oral group nausea and vomiting observed in 6(12.5%) and 6(12.5%) patients followed by abdominal cramps 5(10.4%). In vaginal group 16(33.3%) had abdominal cramps followed by nausea in 3(6.3%)

GRAPHICAL REPRESENTATION OF DISTRIBUTION OF PATIENTS ACCORDING TO CERVICAL DILATION (MM)



It is observed in the sublingual group, majority of patients 20(41.7%) had cervical dilation of 4mm followed by 16(33.3%) had cervical dilation of 3 mm. It is observed in the oral group majority of patients 26(54.2%) had cervical dilation of 3mm followed by 10(20.8%) had cervical dilation of 4mm and 2mm.It is observed in the vaginal group, majority of patients 25(52.1%) had cervical dilation of2mm followed by 16(33.3%) had cervical dilation of 3mm

GRAPHICAL REPRESENTATION OF DISTRIBUTION OF PATIENTS ACCORDING TO TIME DURATION



The mean duration of procedure was 10.33 minutes in sublingual group, 11.38 minutes in oral group and 11.68 minutes in vaginal group, which is significant (p=0.045).

The results are consistent with studies conducted by Saxena P et al.,(2007) Shagufta P et al.,(2011).

DISCUSSION

In numerous studies prostaglandins assessed to have efficacy for cervical priming before procedures.[92, 93] Misoprostol is an agent of choice for cervical ripening because of its features like stability at room temperature, cheap, easily available in different dosage forms. As mifepristone is expensive, it is desirable to develop regimen without mifepristone.[94]. The present study observed sublingual administration of misoprostol is better than oral than vaginal route.

In our study majority of patients were in the age group of 21-25yrs in the sublingual group, 26-30yrs in the oral group and 21-25yrs in the vaginal group. The mean age was 25.3, 25.9 and 25.5 respectively, which is comparable to Shagufta P et al., (2011) (27.7 Yrs, 27.3yrs, 26.8 Yrs respectively in sublingual , oral and vaginal group), Saxena P et al., (2007) (26.6, 25.6, 26.8yrs respectively in sublingual, oral and vaginal group), Lawrie A et al (25.5yrs and 26.4 yrs respectively in oral and vaginal group), Oppegaard K et al., (2006)[6,72] (27.7yrs and 28.1 yrs respectively in oral and vaginal group). However, the mean age in Ashok PW et al., (2003) (20.1 and 20.4 respectively in oral and vaginal group) Ngai SW et al., (1999) (23.4 and 22.2 respectively in oral and vaginal group) is not comparable because of selection of only nulligravida women in these studies.[68, 71]

In the present study, all were multigravida in all groups (144/144 were multigravida), where as in other studies both multigravida and primigravida were included like in Shagufta P et al.,(2010), Saxena P et al.,(2007), Lawrie A et al.,(1996) (33 and 67 in oral group , 30 and 70 in vaginal group, Primigravida and multigravida respectively), Oppegaard K et al.,(2006) (49 and 51 in oral group , 51 and 49 in the vaginal group, primigravida and multigravida respectively). In the Ashok PW et a.,(2003) (20.1 and 20.4 yrs in oral and vaginal respectively), Ngai SW et al.,(1999) (23.4 and 22.2 yrs in oral and vaginal group respectively) mean age was less because their selection criteria was nulligravida.[68, 71]

Mean cervical dilation in our study was better in sublingual group than oral group than vaginal group with mean cervical dilation 3.15 mm, 2.92mm and 2.44 mm respectively (Initial dilator that passes through os without any resistance). In our study we found cervical dilation is significantly higher with sublingual route than oral or vaginal route. Similar results were shown with Shagufta et al, Saxena et al study, Faundes A et al, Inal MM et al studies. In shagufta et al study misoprostol was given 12 hour prior in oral group and 3 hour prior in sublingual and vaginal group showed, cervical dilation with sublingual route is

better than oral and vaginal route (9.1mm, 8.1 and 4.8 mm respectively). Faundes A et al study compared rate of complete abortion by three different routes i.e. sublingual, oral, vaginal routes using 800 microgram misoprostol, 6th hourly, 8th hourly, or 12 hourly and they concluded that sublingual and oral route of administration better than vaginal route as it caused better cervical dilation leading to complete abortion. In a study by Inal et al 120 women were divided in four groups and given 200 microgram misoprostol or placebo orally and vaginally, 10hour prior to the procedure and results showed that oral misoprostol (8 mm dilation) is better route than vaginal (<8mm) route . The more dilation in this study may be attributed to more time duration as compared to our study and one more study done by Saxena et al over 120 women using 400 microgram misoprostol by three different routes i.e. sublingually, vaginally and orally and concluded that sublingual route is better than oral than vaginal route of administration.

Our data not correlating with Oppegaard et al,.(2006), Lawrie et al Von Hertzen H et al,studies. In Oppegaard et al,.(2006) , they had given misoprostol 12 hrs prior to the procedure resulting in cervical dilation of 6.2mm and 6.5mm in oral and vaginal route respectively. In addition, sample size was small in most studies except Oppegaard K et al where sample size was calculated on the primary outcome of cervical dilation with assumption of type 1 error of 0.05 and a power of 0.90. In Lawrie et al study misoprostol was given 12 hrs prior in oral group and 3 hrs prior in vaginal group and dosage was 800 microgram misoprostol was used vaginally., resulting in 6.9 mm and 7 mm was cervical dilation respectively in oral and vaginal group. Dilation was more as compared to our study because of more time duration in oral group and more dosage i.e. 800 microgram vaginally as compared to 400 microgram in our study. Von Hertzen H et al done over 2064 women, they compared sublingual and vaginal route by giving 800 microgram 3 hr prior and 12 hr prior. Study showed vaginal route administration of misoprostol is better than sublingual in causing complete abortion. In a study done by carbonell, JL et al misoprostol was given 8hr prior, but this study concluded vaginal route better than oral route.

In our study loose motion was seen only in sublingual group and vomiting was more in oral group and abdominal cramp was more in vaginal group. Nausea is seen all groups more in oral group. Our data is different than that of Lawrie A et al., (1996), Oppegaard K et al., (2006), carbonell JL et al studies. In Lawrie A et al., (1996) 400 microgram misoprostol was used with pretreatment interval of 12 hrs in oral route and 3 hrs in vaginal route and showed that oral route had more pain, more incomplete abortion and heavier preoperative bleeding as compared to vaginal route. In Oppegaard K et al., (2006) oral misoprostol was given 12 hours prior to surgical abortion concluded that oral group had more gastrointestinal side effects and more bleeding (OR:10.4, 95% CI± 5.2 to 20.8). Our study is consistent with shagufta et al (2011), Ashok PW et al, Saxena p (2007) and Ngai et al. In shagufta study they observed that pain score was significantly less with sublingual route and loose motions, nausea, vomiting seen mainly in oral group and vaginal bleeding was more with vaginal route. In a study conducted by Saxena P., (2007) showed nausea, vomiting more in sublingual and oral group than vaginal group. In Ashok PW et al., (2003) a comparative study between oral and vaginal misoprostol as a cervical priming agent before first trimester surgical abortion showed that there is no significant difference in oral and vaginal groups, but women receiving vaginal misoprostol experienced more tiredness (OR: 0.2, 95% CI± 0.1 -0.7), where as women receiving oral misoprostol experienced more nausea (OR:3.9, 95% CI± 1.3-11.2). Ngai SW et al., (1999) a comparative study between oral and vaginal misoprostol as a cervical priming agent before first trimester surgical abortion, showed oral group likely to experience more nausea. It is the

first study to show that oral misoprostol is effective for cervical priming given 3 hours prior to the procedure.

The present study observed sublingual administration of misoprostol is better than oral than vaginal route. This difference could be due to differences in absorption kinetics and our results could be arrtibuted to anesthesia used i.e.in our study majority of patients undergone surgical abortion under intravenous sedation (IVS) i.e. in 68.8 % patients & general anesthesia was given only in 17.4% of patients . Duration of procedure was less in sublingual group than oral than vaginal group, this is attributed to more cervical dilation by sublingual route of administration.

Our study showed sublingual route has better dilation may be because of buccal mucosa being very vascular, tablet dissolves within 15 minutes of administration. Advantage of route is it avoids ingestion of water.

CONCLUSION

This study demonstrated that 400 microgram misoprostol given 4 hour prior to first trimester surgical abortion is a better effective and safe cervical ripening agent by sublingual route as compared to vaginal and oral routes.

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